

We claim:

1. An enteric fluoxetine pellet comprising a) a core consisting of fluoxetine and one or more pharmaceutically acceptable excipients; b) an optional separating layer comprising a non-reducing sugar and one or more pharmaceutically acceptable excipients; c) an enteric layer comprising hydroxypropylmethylcellulose acetate succinate (HPMCAS) and one or more pharmaceutically acceptable excipients; d) an optional finishing layer.

2. A pellet of claim 1 wherein the HPMCAS is partially neutralized with ammonium ions to the degree that from about 0% to about 25% of the succinic acid groups are neutralized.

3. A pellet of claim 2 wherein the HPMCAS is partially neutralized to the degree that from about 0% to about 15% of the succinic acid groups are neutralized.

4. A pellet of claim 1 wherein the separating layer is present.

5. A pellet of claim 1 wherein the average particle size of the fluoxetine is about 50 μm or less.

6. A pellet of claim 5 wherein the core comprises an inert core on which the fluoxetine is deposited as a layer comprising in addition a pharmaceutically acceptable excipient.

7. A pellet of claim 6 wherein the separating layer is present.

8. A pellet of claim 7 wherein the HPMCAS is partially neutralized with ammonium ions to the degree that from about 0% to about 25% of the succinic acid groups are neutralized.

9. A pellet of claim 4 wherein the separating layer comprises a pharmaceutically acceptable sugar.

10. A pellet of claim 9 wherein the sugar is sucrose.

11. A process for preparing an enteric fluoxetine pellet comprising a) providing a core consisting of fluoxetine and one or more pharmaceutically acceptable excipients; b) optionally, applying to the core a separating layer comprising a non-reducing sugar and one or more pharmaceutically acceptable excipients; c) applying an enteric layer comprising HPMCAS and one or more pharmaceutically acceptable excipients, wherein the HPMCAS is supplied as an aqueous solution or suspension and the application takes place in an apparatus of the fluid bed type; d) optionally, applying a finishing layer.

12. A process of claim 11 wherein the HPMCAS is fully or partially neutralized with ammonium ions.

13. A process of claim 12 wherein the HPMCAS is neutralized to the degree that from about 25% to about 100% of the succinic acid groups are neutralized.

14. A process of claim 11 wherein the separating layer is applied.

15. A process of claim 14 wherein the separating layer comprises a pharmaceutically acceptable sugar.

16. A process of claim 15 wherein the sugar is sucrose.

17. A process of claim 11 wherein the core is prepared by applying fluoxetine and one or more pharmaceutically acceptable excipients to an inert core.

18. A process of claim 17 wherein the separating layer is applied and comprises a pharmaceutically acceptable sugar.

19. A formulation of claim 1 containing 20–100 mg base equivalent of fluoxetine.

20. A formulation of claim 1 containing about 80–90 mg base equivalent of fluoxetine.

21. A formulation of claim 1 containing about 90 mg base equivalent of fluoxetine.

22. A formulation of claim 19 wherein the fluoxetine is present as fluoxetine hydrochloride.

23. A formulation of claim 20 wherein the fluoxetine is present as fluoxetine hydrochloride.

24. A formulation of claim 21 wherein the fluoxetine is present as fluoxetine hydrochloride.

25. A gelatin capsule containing the formulation of claim 1.

26. A gelatin capsule containing the formulation of claim 24.

27. A formulation of claim 1 containing the following:

Cores		
Sucrose-starch nonpareils, 30–35 mesh		100–150 mg
Fluoxetine layer		
Fluoxetine hydrochloride		100.5–100.8 mg
Sucrose		20–30 mg
Separating layer		
Hydroxypropylmethylcellulose		4–12 mg
Sucrose		15–35 mg
Talc, 500 mesh		25–60 mg
Enteric layer		
HPMCAS-LF		60–90 mg
Triethyl citrate		10–20 mg
Talc, 500 mesh		15–25 mg
Finishing layer		
Color mixture white (HPMC + titanium dioxide)		35–55 mg
HPMC		5–15 mg
Talc		Trace.

28. A gelatin capsule containing the formulation of claim 24.

29. A formulation according to claim 1 wherein the formulation additionally contains pindolol.

30. A method of treating people suffering from depression, obsessive-compulsive disorder, bulimia, pain, obsessive-compulsive personality disorder, post-traumatic stress disorder, hypertension, atherosclerosis, anxiety, anorexia nervosa, panic, social phobia, stuttering, sleep disorders, chronic fatigue, Alzheimer's disease, alcohol abuse, appetite disorders, weight loss, agoraphobia, improving memory, amnesia, smoking cessation, nicotine withdrawal symptoms, disturbances of mood and/or appetite associated with pre-menstrual syndrome, depressed mood and/or carbohydrate craving associated with pre-menstrual syndrome, disturbances of mood, disturbances of appetite or disturbances which contribute to recidivism associated with nicotine withdrawal, circadian rhythm disorder, borderline personality disorder, hypochondriasis, pre-menstrual syndrome (PMS), late luteal phase dysphoric disorder, premenstrual dysphoric disorder, trichotillomania, symptoms following discontinuation of other antidepressants, aggressive/intermittent explosive disorder, compulsive gambling, compulsive spending, compulsive sex, psychoactive substance use disorder, sexual disorder, schizophrenia, premature ejaculation, or psychiatric symptoms selected from stress, worry, anger, rejection sensitivity, and lack of physical energy comprising administering a formulation of claim 1.

31. A method of claim 30 employing a formulation containing 20–100 mg base equivalent of fluoxetine.

32. A method of claim 30 employing a formulation containing about 90 mg base equivalent of fluoxetine.

33. A method of claim 30 wherein the fluoxetine is present as fluoxetine hydrochloride.

34. A method of claim 31 wherein the fluoxetine is present as fluoxetine hydrochloride.

35. A method of claim 32 wherein the fluoxetine is present as fluoxetine hydrochloride.

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36. A method of claim 30 employing a formulation containing the following:

<u>Cores</u>		
Sucrose-starch nonpareils, 30-35 mesh	100-150	mg
<u>Fluoxetine layer</u>		
Fluoxetine hydrochloride	100.5-100.8	mg
Sucrose	20-30	mg
Hydroxypropylmethylcellulose	10-15	mg
<u>Separating layer</u>		
Hydroxypropylmethylcellulose	4-12	mg
Sucrose	15-35	mg
Talc, 500 mesh	25-60	mg
<u>Enteric layer</u>		
HPMCAS-LF	60-90	mg
Triethyl citrate	10-20	mg

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<u>Finishing layer</u>		15-25	mg
5	Color mixture white (HPMC + titanium dioxide)	35-55	mg
	HPMC	5-15	mg
	Talc	Trace.	

37. A method of claim 30 of treating people suffering from pain, further comprising the coadministration of morphine, codeine or dextropropoxyphene.

38. A method of claim 37 employing a formulation containing 20-100 mg base equivalent of fluoxetine.

39. A method of claim 37 employing a formulation containing about 90 mg base equivalent of fluoxetine.

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